

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (original): A method of treating acne in a human in need thereof comprising administering systemically to said human a tetracycline compound in an amount that is effective to treat acne but has substantially no antibiotic activity, without administering a bisphosphonate compound.

Claim 2 (original): A method according to Claim 1, wherein said acne is acne vulgaris, cystic acne, acne atrophica, bromide acne, chlorine acne, acne conglobata, acne cosmetica, acne detergentica, epidemic acne, acne estivalis, acne fulminans, halogen acne, acne indurata, iodide acne, acne keloid, acne mechanica, acne papulosa, pomade acne, premenstrual acne, acne pustulosa, acne rosacea, acne scorbutica, acne scrofulosorum, acne urticata, acne varioliformis, acne venenata, propionic acne, acne excoriee, gram negative acne, steroid acne, or nodulocystic acne.

Claims 3-22 (canceled).

Claim 23 (original): A method according to Claim 1, wherein said tetracycline compound is a non-antibiotic tetracycline compound.

Claim 24 (original): A method according to Claim 23, wherein said non-antibiotic tetracycline compound is:

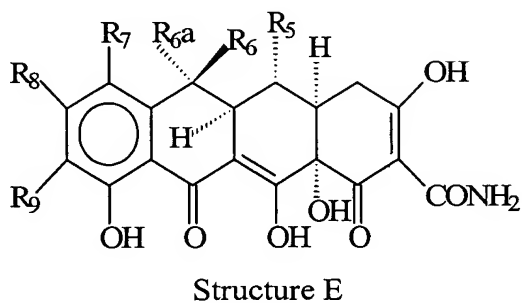
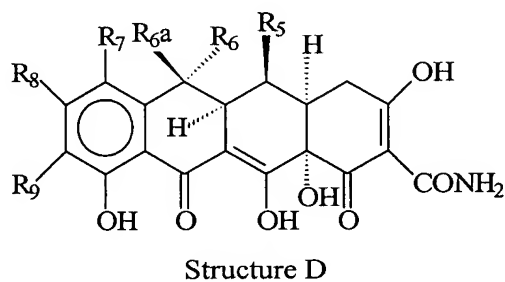
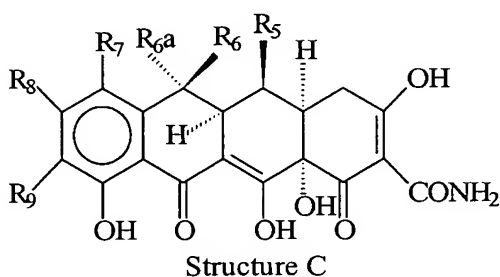
4-de(dimethylamino)tetracycline (CMT-1),

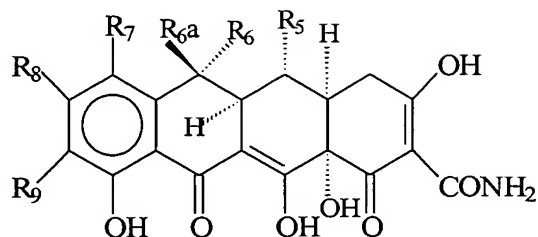
tetracyclonitrile (CMT-2),

6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline (CMT-3),

4-de(dimethylamino)-7-chlorotetracycline (CMT-4),  
tetracycline pyrazole (CMT-5)  
4-hydroxy-4-de(dimethylamino)tetracycline (CMT-6),  
4-de(dimethylamino)-12 $\alpha$ -deoxytetracycline (CMT-7),  
6- $\alpha$ -deoxy-5-hydroxy-4-de(dimethylamino)tetracycline (CMT-8),  
4-de(dimethylamino)-12 $\alpha$ -deoxyanhydrotetracycline (CMT-9), or  
4-de(dimethylamino)minocycline (CMT-10).

Claim 25 (original): A method according to Claim 23, wherein the non-antibiotic tetracycline compound is selected from the group consisting of:





Structure F

wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl; R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, diazonium, di(lower alkyl)amino and  $RCH(NH_2)CO$ ;

R is hydrogen or lower alkyl; and

pharmaceutically acceptable salts thereof; with the following provisos:

when either R7 and R9 are hydrogen then R8 must be halogen; and

when R6-a, R6, R5 and R9 are all hydrogen and R7 is hydrogen, amino, nitro, halogen, dimethylamino or diethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is hydrogen, amino, nitro, halogen or diethylamino, then R8 is halogen; and

when R6-a is methyl, R6 is hydroxyl, R5, R7 and R9 are all hydrogen, then R8 must be halogen; and

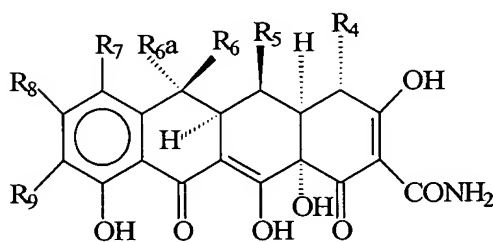
when R6-a, R6 and R5 are all hydrogen, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 is hydrogen, R5 is hydroxyl, R9 is methylamino and R7 is

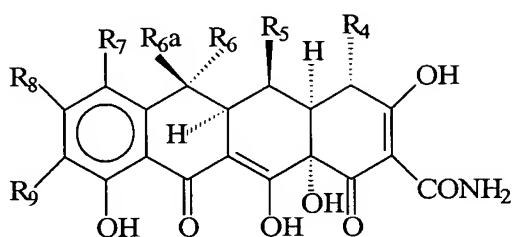
dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6, R5 and R9 are all hydrogen and R7 is cyano, then R8 must be halogen.

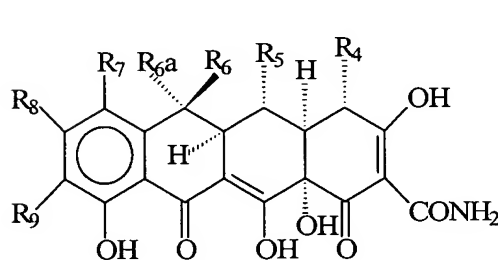
Claim 26 (original): A method according to Claim 23, wherein the non-antibiotic tetracycline compound is selected from the group consisting of:



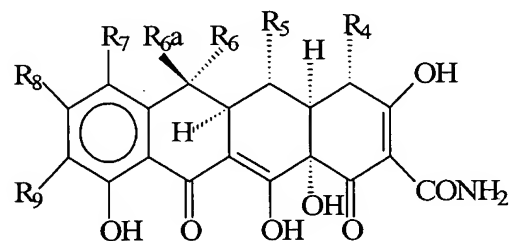
Structure G



Structure H



Structure I



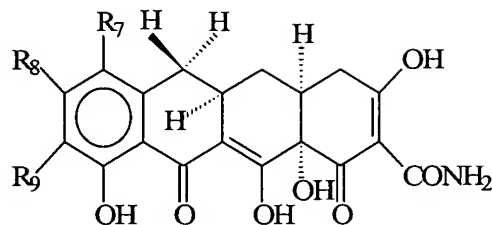
Structure J

wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, and di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;  
R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;  
R4 is selected from the group consisting of NOH, N-NH-A, and NH-A,  
where A is a lower alkyl group;  
R8 is selected from the group consisting of hydrogen and halogen;  
R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino,  
hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, di(lower alkyl)amino  
and RCH(NH<sub>2</sub>)CO;  
R is hydrogen or lower alkyl; and  
pharmaceutically acceptable salts thereof; with the following provisos:  
when R4 is NOH, N-NH-alkyl or NH-alkyl and R7, R6-a, R6, R5, and R9 are all  
hydrogen, then R8 must be halogen; and  
when R4 is NOH, R6-a is methyl, R6 is hydrogen or hydroxyl, R7 is halogen, R5  
and R9 are both hydrogen, then R8 must be halogen; and  
when R4 is N-NH-alkyl, R6-a is methyl, R6 is hydroxyl and R7, R5, R9 are all  
hydrogen, then R8 must be halogen; and  
when R4 is NH-alkyl, R6-a, R6, R5 and R9 are all hydrogen, R7 is hydrogen, amino,  
mono(lower alkyl)amino, halogen, di(lower alkyl)amino or hydroxyl, then R8 must be  
halogen; and  
when R4 is NH-alkyl, R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl,  
and R7 is mono(lower alkyl)amino or di(lower alkyl)amino, then R8 must be halogen; and  
when R4 is NH-alkyl, R6-a is methyl, R6 is hydroxy or hydrogen and R7, R5, and R9  
are all be hydrogen, then R8 must be halogen.

Claim 27 (original): A method according to Claim 23 wherein the non-antibiotic  
tetracycline compound is selected from the group consisting of:

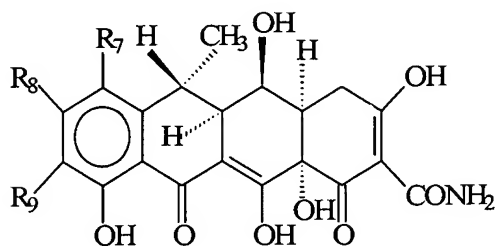


Structure K

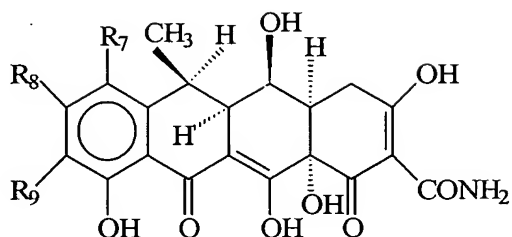
wherein: R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	acylamino
dimethylamino	hydrogen	diazonium
dimethylamino	chloro	amino
hydrogen	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
monoalkylamino	chloro	amino
nitro	chloro	amino
dimethylamino	chloro	acylamino
dimethylamino	chloro	dimethylamino
hydrogen	hydrogen	dimethylamino
dimethylamino	hydrogen	hydrogen

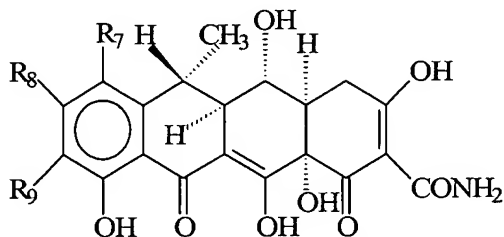
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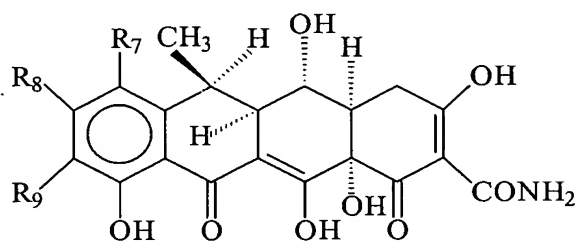
Structure L



Structure M



Structure N



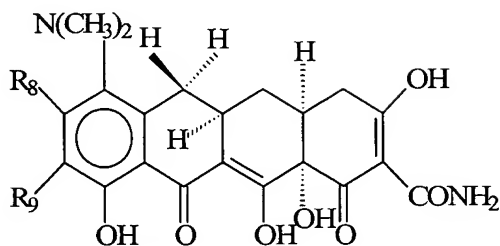
Structure O

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro

dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	acylamino
hydrogen	hydrogen	diazonium
hydrogen	hydrogen	dimethylamino
diazonium	hydrogen	hydrogen
ethoxythiocarbonylthio	hydrogen	hydrogen
dimethylamino	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
hydrogen	chloro	amino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
monoalkylamino	chloro	amino
nitro	chloro	amino

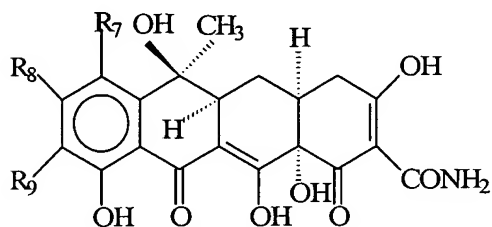
and



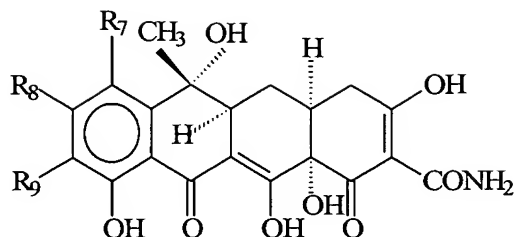
Structure P

wherein: R8 is hydrogen or halogen and R9 is selected from the group consisting of nitro, (N,N-dimethyl)glycylamino, and ethoxythiocarbonylthio; and





Structure Q



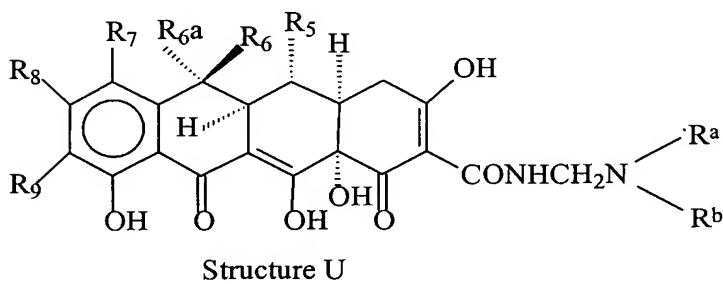
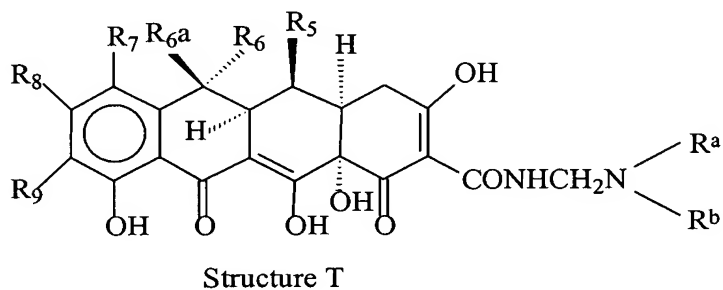
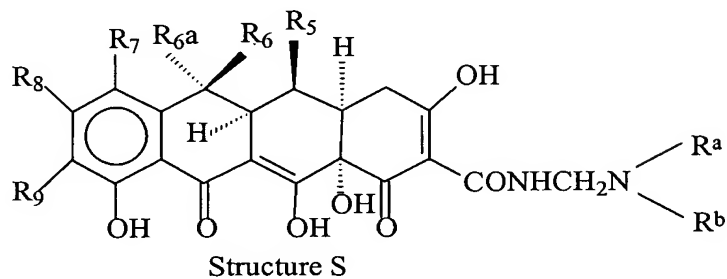
Structure R

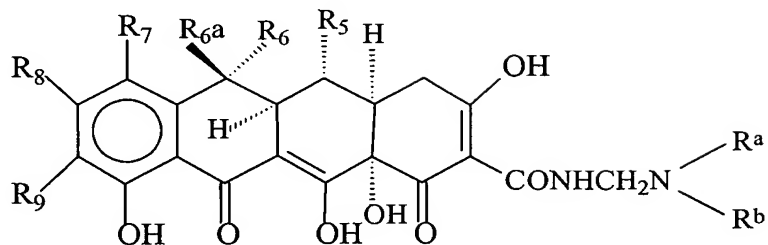
wherein: R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
amino	hydrogen	hydrogen
nitro	hydrogen	hydrogen
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
bromo	hydrogen	hydrogen
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
diethylamino	hydrogen	hydrogen
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	methylamino
dimethylamino	hydrogen	acylamino
dimethylamino	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
hydrogen	chloro	amino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
monoalkylamino	chloro	amino
nitro	chloro	amino

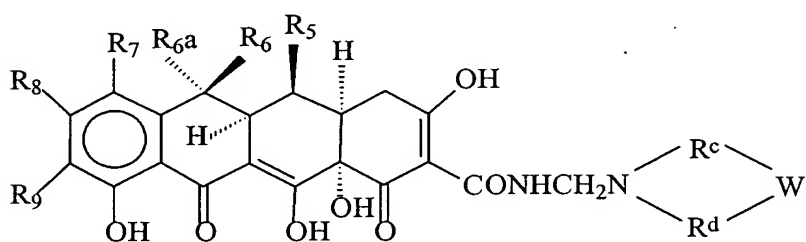
and pharmaceutically acceptable salts thereof.

Claim 28 (original): A method according to Claim 23, wherein the non-antibiotic tetracycline compound is selected from the group consisting of:

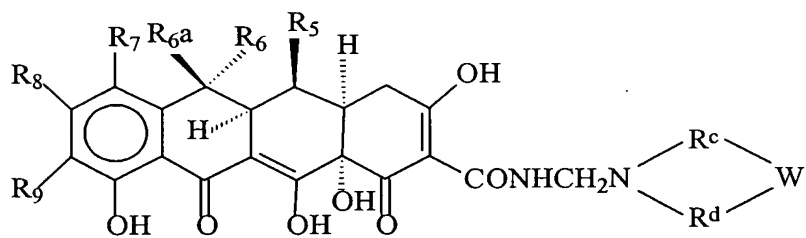




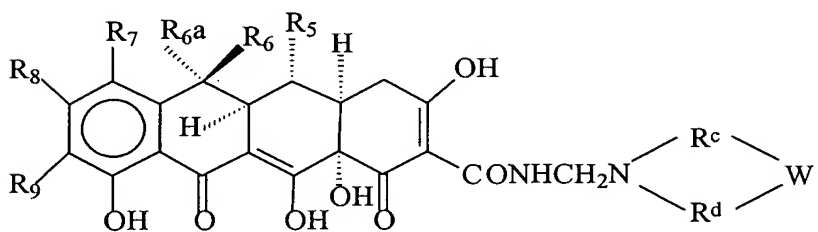
Structure V



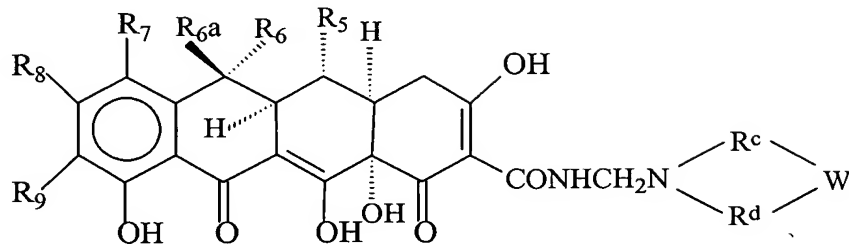
Structure W



Structure X



Structure Y



Structure Z

wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl; R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, diazonium, di(lower alkyl)amino and  $RCH(NH_2)CO$ ;

R is hydrogen or lower alkyl;

$R^a$  and  $R^b$  are selected from the group consisting of hydrogen, methyl, ethyl, n-propyl and 1-methylethyl with the proviso that  $R^a$  and  $R^b$  cannot both be hydrogen;

$R^c$  and  $R^d$  are, independently,  $(CH_2)_nCHR^e$  wherein n is 0 or 1 and  $R^e$  is selected from the group consisting of hydrogen, alkyl, hydroxy, lower( $C_1$ - $C_3$ ) alkoxy, amino, or nitro; and,

W is selected from the group consisting of  $(CHR^e)_m$  wherein m is 0-3 and said  $R^e$  is as above, NH,  $N(C_1$ - $C_3)$  straight chained or branched alkyl, O, S and  $N(C_1$ - $C_4)$  straight chain or branched alkoxy; and,

pharmaceutically acceptable salts thereof.

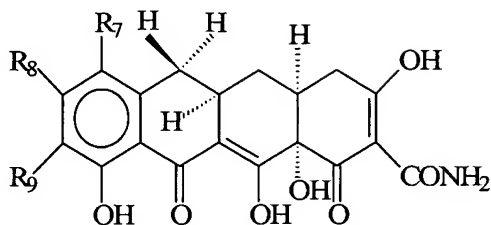
Claim 29 (original): A method according to Claim 16, wherein the non-antibiotic tetracycline compound selected from the group consisting of structures S-Z has the following provisos:

- when either R7 and R9 are hydrogen then R8 must be halogen; and
- when R6-a, R6, R5 and R9 are all hydrogen and R7 is hydrogen, amino, nitro, halogen, dimethylamino or diethylamino, then R8 must be halogen; and
- when R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is hydrogen, amino, nitro, halogen or diethylamino, then R8 is halogen; and
- when R6-a is methyl, R6 is hydroxyl, R5, R7 and R9 are all hydrogen, then R8 must be halogen; and
- when R6-a, R6 and R5 are all hydrogen, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and
- when R6-a is methyl, R6 is hydrogen, R5 is hydroxyl, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and
- when R6-a is methyl, R6, R5 and R9 are all hydrogen and R7 is cyano, then R8 must be halogen.

Claim 30 (original): A method according to Claim 1, wherein said tetracycline compound has a photoirritancy factor of less than the photoirritancy factor of doxycycline.

Claim 31 (original): A method according to Claim 1, wherein said tetracycline compound has a photoirritancy factor from about one to about two.

Claim 32 (original): A method according to Claim 31, wherein said tetracycline compound has a general formula:

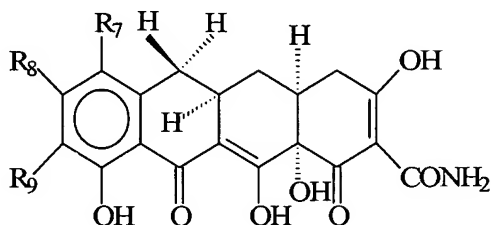


Structure K

wherein R<sub>7</sub>, R<sub>8</sub>, and R<sub>9</sub> taken together are, respectively, hydrogen, hydrogen and dimethylamino.

Claim 33 (original): A method according to Claim 1, wherein said tetracycline compound has a photoirritancy factor from about 1.0 to about 1.2.

Claim 34 (original): A method according to Claim 33, wherein said tetracycline compound is selected from the group consisting of:

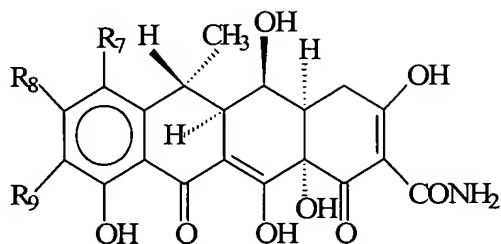


Structure K

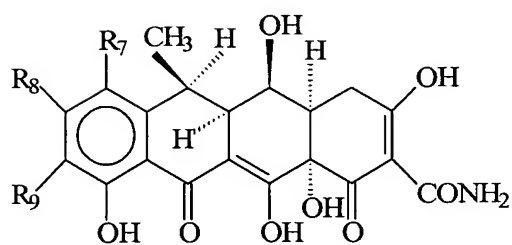
wherein R<sub>7</sub>, R<sub>8</sub>, and R<sub>9</sub> taken together in each case, have the following meanings:

R <sub>7</sub>	R <sub>8</sub>	R <sub>9</sub>
hydrogen	hydrogen	amino
hydrogen	hydrogen	palmitamide

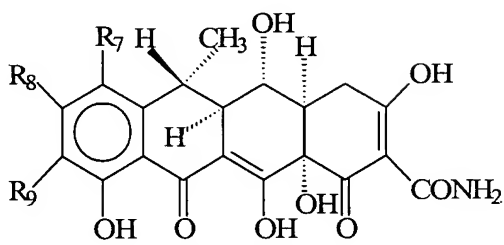
and



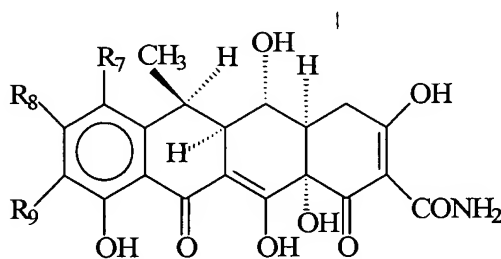
Structure L



Structure M



Structure N



Structure O

wherein R7, R8, and R9 taken together in each case, have the following meanings:

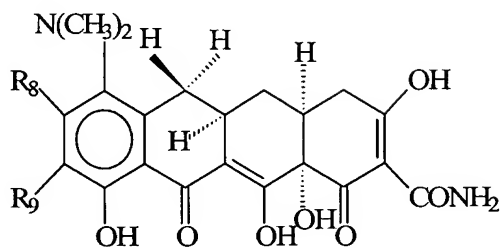
R7

R8

R9

hydrogen	hydrogen	acetamido
hydrogen	hydrogen	dimethylaminoacetamido
hydrogen	hydrogen	nitro
hydrogen	hydrogen	amino

and



Structure P

wherein R8, and R9 taken together are, respectively, hydrogen and nitro.

Claim 35 (original): A method according to Claim 1, wherein said systemic administration is oral administration, intravenous injection, intramuscular injection, subcutaneous administration, transdermal administration or intranasal administration.

Claim 36 (original): A method of treating acne in a human in need thereof comprising administering to said human an effective amount of a non-antibiotic tetracycline compound without administering a bisphosphonate compound.

Claim 37 (canceled).

Claim 38 (original): A method according to Claim 36, wherein said administration is systemic administration.

Claims 39-45 (canceled).